

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 9516-207-228	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/35545	International filing date (day/month/year) 06 November 2003 (06.11.2003)	Priority date (day/month/year) 06 November 2002 (06.11.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/44, 31/425, 31/415, 31/40 and US Cl.: 514/301, 339, 373, 387, 412, 417		
Applicant CELGENE CORPORATION		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application

Date of submission of the demand 04 June 2004 (04.06.2004)	Date of completion of this report 13 March 2005 (13.03.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Raymond J. Henley III Telephone No. 571-272-0600

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-65 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 66-73, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-32 meet the criteria under PCT Article 33(2) for novelty because the prior art fails to teach the presently claimed methods for treating, managing or preventing a specific cancer or disease associated with undesired angiogenesis or for reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a specific cancer or radiation therapy or a kit useful in such methods.

Claims 1-32 meet the criteria under PCT Article 33(3) for inventive step because the prior art fails to teach or suggest the presently claimed methods for treating, managing or preventing a specific cancer or disease associated with undesired angiogenesis or for reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a specific cancer or radiation therapy or a kit useful in such methods.

Claims 1-32 meet the criteria under PCT Article 33(4) because the presently claimed methods for treating, managing or preventing a specific cancer or disease associated with undesired angiogenesis, for reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a specific cancer or radiation therapy and a kit useful in such methods would have applicability in the medical industry.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-18 and 21-26 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because of the following reasons.

The present specification is evaluated by the Examiner as directed by the Court in *In re Marzocchi et al.*, 169 USPQ 367 (CCPA 1971):

"Specification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

Here, the objective truth that all specific types of cancer may be treated is doubted because while the state of the art is relatively high with regard to the treatment of specific cancer types, the state of the art with regard to treating cancer broadly is underdeveloped. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against all cancer types.

Also, the objective truth that the claimed diseases can be prevented is doubted because the burden of enabling the prevention of a disease would be much greater than that of enabling the treatment of a disease. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing the claimed diseases or how a patient could be kept from every being susceptible to these diseases. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agents for preventing the claimed diseases.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified active could actually prevent the claimed diseases by simply administering, by any method, an amount of the claim specified active agents. The specification fails to enable one of ordinary skill in the art to practice the prevention of the claimed diseases.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of absolute success. Since absolute success is not reasonably possible with most diseases, especially those having etiologies and pathophysiological manifestations as complex/poorly understood as the presently claimed diseases, the specification, which lacks an objective showing that any of the claimed diseases can actually be prevented, is viewed as lacking an adequate written description of the same.